Journal of Surgical Oncology 1997;66:141–147

REVIEW ARTICLE

Intracavitary Brachytherapy in the Treatment of Gynecologic Neoplasms

PATRICIA J. EIFEL, MD*
Department of Radiation Oncology, The University of Texas, M.D. Anderson Cancer Center, Houston, Texas

Modern intracavitary brachytherapy carefully combined with megavoltage external beam radiotherapy is responsible for the high cure rates achieved with radiation treatment of invasive cervical cancers. Pelvic disease recurrence is rare after treatment of patients with tumors <5 cm in diameter, and even patients with massive tumors 8–10 cm in diameter are cured in 30–50% of cases. Inoperable adenocarcinomas of the endometrium and superficial cancers of the vagina are also effectively treated with intracavitary irradiation. The relative radioresistance of the uterus and vagina, physical advantages resulting from exploitation of the inverse square law, and the radiobiological advantages of low dose rate radiation have combined to make intracavitary irradiation a critical tool in the management of many gynecologic neoplasms.

J. Surg. Oncol. 1997;66:141–147.

KEY WORDS: cervical cancer; endometrial cancer; radiotherapy

INTRODUCTION

Encapsulated radium sources were first placed in the uterine cavity to treat gynecologic cancers shortly after Marie Curie's discovery more than a century ago. Early reports documented dramatic responses of cervical and endometrial cancers to radium treatment and revealed that the uterus and vagina could tolerate relatively high doses of radiation without serious morbidity. Radiation biologists eventually determined that the favorable therapeutic ratio of radium treatment was due, in part, to the relatively slow rate at which the treatment was delivered, permitting greater repair of radiation damage in normal tissues than in the tumor.

Appreciation of the efficacy of intracavitary radium treatment led to the design of specialized applicators, refinements in methods of dose specification, and increasing reports of the successful treatment of cervical and uterine body cancers with radium [1]. In the mid-1950s, the development of machines that could deliver deeply penetrating external-beam irradiation provided a means of treating regional disease effectively, complimenting intracavitary treatment and leading to the high pelvic control and cure rates that are now achieved with radiation treatment of invasive cervical cancers. Since then, prospective and retrospective studies of patients treated for gynecologic neoplasms have enabled clinicians to improve their understanding of the indications for intracavitary irradiation and to refine methods of intracavitary brachytherapy and its combination with external-beam irradiation. Technological advances have also improved the safety of source handling and have reduced the exposure of physicians and nursing personnel to radiation during intracavitary treatments.

CANCER OF THE CERVIX

The advantages of intracavitary irradiation have been exploited most effectively in the treatment of invasive carcinomas of the cervix. Reports of the results of treatment from a number of large series of patients reveal

*Correspondence to: Patricia J. Eifel, MD, Department of Radiation Oncology, Box 97, The University of Texas, M.D. Anderson Cancer Center, 1515 Holcombe Blvd., Houston, TX, 77030. Telephone: (713) 792-3444; Fax: (713) 792-3642.

Accepted 15 May 1997

TABLE I. Relationship Between Tumor Diameter and Disease Control Rates at 5 Years for 1526 Patients Treated for FIGO Stage IB Squamous Carcinomas of the Cervix at M. D. Anderson Cancer Center*

Tumor diameter (cm)	Patients	Central disease control	Pelvic disease control	Disease-specific survival
<5	977	99%	97%	88%
5–7.9	451	93%	84%	69%
>8	66	75%	67%	47%
All patients	1526	96%	92%	81%

Includes 32 patients for whom there was no description of tumor diameter.

*Reproduced with permission of Elsevier Science, Inc. from Eifel PJ, Morris M, Wharton JT, et al: The influence of tumor size and morphology on the outcome of patients with FIGO stage IB squamous cell carcinoma of the uterine cervix. Int J Radiat Oncol Biol Phys 29:9–16, 1994.

pelvic disease control rates of more than 95% for patients with Stage IB tumors ⩽4 cm in diameter and of approximately 85% for patients with Stage IB tumors ⩾5 cm in diameter (Table I) [2–4]. Overall survival rates of approximately 80 and 70% are usually reported for patients with Stages I and II disease, respectively (Fig. 1) [2–6]. Several studies have suggested that the outcome of patients treated for bulky stage I and II disease is correlated with the combined central dose of radiation administered with external-beam irradiation and brachytherapy [7–9]. Because the deliverable dose is strongly dependent upon the emphasis placed on intracavitary treatment, these experiences suggest the importance of carefully administered intracavitary treatment to the cure of these patients.

Even patients with massive tumors that are fixed to the pelvic wall can be cured in 40–50% of cases if treatment includes high-dose intracavitary irradiation [5,10]. Several studies have provided evidence of the critical role that intracavitary irradiation plays in the cure of patients with these locally advanced tumors. In a review of patients with FIGO stage IIIB disease included in the Patterns of Care Studies, Lanciano et al. [10] reported a 46% 4-year survival rate in patients treated with intracavitary irradiation vs. 19% for those treated with external-beam irradiation alone ($P < 0.01$). Another study of 1086 patients with stage IIIB disease treated with radiation at The University of Texas M.D. Anderson Cancer Center yielded similar findings; the 5-year survival rate of patients treated with curative intent using external-beam irradiation alone was 21% compared to 44% for those treated with a combination of external-beam and intracavitary irradiation, and survival rates during different treatment eras were strongly correlated with the proportion of patients whose treatment included intracavitary therapy.

Successful treatment requires a careful integration between external beam and intracavitary irradiation. Most patients with loco-regionally advanced disease begin treatment with a course of external-beam irradiation to the pelvis. This treatment is given to sterilize regional and paracervical disease that will receive an inadequate dose of intracavitary irradiation. This initial course of treatment usually causes some regression of bulky exophytic or endocervical tumor, reducing the central tumor to a volume and configuration that can more easily be encompassed in the high-dose region surrounding the intrauterine and intravaginal sources. Patients with smaller tumors may receive intracavitary treatment before pelvic irradiation.

Intracavitary Applicators and Technique

Although a number of different applicator types are used to treat cervical cancers, all consist of hollow repositories for placement of radioactive sources in the uterine cavity and vagina (Fig. 2). A tube called a ''tandem'' or ''stem'' is usually placed in the uterus and combined with one of a variety of vaginal applicators that permit placement of sources adjacent to the cervix in the vaginal apex. The curvature of the tandem and size of the vaginal applicators are selected to match the patient's anatomy and to optimize the relationship between the sources, tumor, and critical structures. Moistened vaginal packing is used to secure the position of the applicators and to pack the bladder and rectum away from the vaginal sources. Because optimal positioning of the applicators and vaginal packing cannot be achieved in a tense patient, the procedure is usually performed under anesthesia. The features analyzed to determine the quality of a placement (using a Fletcher-Suit-Delclos applicator) are demonstrated in Figure 2. In particular, the vaginal ovoids should be against the cervical portio (marked with radioopaque seeds) and should generally be bisected by the tandem on the lateral X-ray view. The tandem should generally be in a mid position in the pelvis. Correct positioning of the applicator should be confirmed with orthogonal pelvic radiographs while the patient is still anesthetized, and the applicator should be repositioned if the placement is unsatisfactory.

Until the late 1970s, most gynecologic intracavitary radiotherapy was delivered using sealed encapsulated sources of ^{226}Ra. Although the long half-life of radium (1600 years) is advantageous, the radon gas produced as one of the byproducts of its radioactive decay poses a potential hazard from accidental failure of the source seal. For this reason, most gynecologic intracavitary radiotherapy is now performed with ^{137}Cs, an artificially produced isotope with a half-life of approximately 30 years. The dose distributions are similar for radium and cesium sources that have a comparable configuration and filtration. However, because of its shorter half-life, the

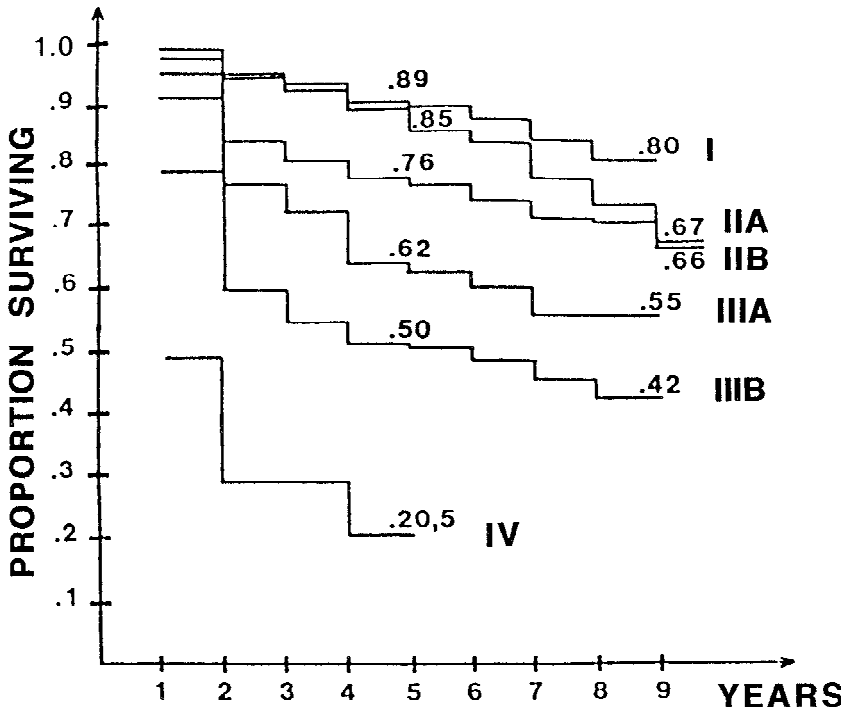

Fig. 1. Survival rates of 1383 patients treated with radiotherapy for FIGO stage I–IVA carcinomas of the uterine cervix. Most patients were treated with a combination of external beam and intracavitary irradiation according to G.H. Fletcher guidelines. (From: Horiot JC, Pigneux J, Pourquier H, et al.: Radiotherapy alone in carcinoma of the intact uterine cervix according to G.H. Fletcher guidelines: A French cooperative study of 1383 cases. Int J Radiat Oncol Biol Phys 14:605–611, 1988, with permission.)

activity of cesium sources must be corrected annually for radioactive decay.

In the 1960s, the radiation exposure to medical personnel during intracavitary placements was decreased considerably by the development of afterloading applicators that were loaded with radioactive sources after the correct positioning had been confirmed and the patient was returned to her hospital room. With more recently developed remote afterloading devices that load and unload the applicators by computer control, personnel exposure is negligible.

Radiation Dose

The favorable therapeutic ratio achieved with intracavitary irradiation of the cervix (and with all brachytherapy techniques) depends, in a large part, on the inverse square law that governs the distribution of radiation around a point source. Because the dose of radiation declines in proportion to the square of the distance from the point source of radioactive material, sources placed in the uterus and vagina deliver a much higher dose to the cervix and upper vagina than to more distant normal tissues. Increases of as little as 2–3 mm in the distance between the sources and normal tissues such as bladder and rectum may result in clinically important decreases in the doses of radiation that reaches these structures, emphasizing the importance of excellent placement and packing of the system.

Unlike interstitial implants, which deliver a relatively homogeneous dose to the treatment volume, intracavitary implants produce a rather steep dose gradient within the tumor. However, the success of intracavitary therapy in controlling even bulky cervical tumors suggests that this dose gradient is not only acceptable but may even be beneficial.

Because the dose delivered with an intracavitary implant is heterogeneous, the methods used to describe and specify treatment are different from those used for interstitial brachytherapy. Although a number of methods have been devised to describe intracavitary doses, most practitioners in the United States use variations of the Manchester system. Under this system, the dose delivered to a paracentral reference point (‘‘Point A’’) is used to describe the intensity of treatment to the central tumor. Doses are also specified to points on the pelvic wall and to normal tissue reference points on the anterior rectal and posterior bladder walls. Most clinicians place Point A 2 cm lateral and superior to the external os of the cervix. The total dose delivered to Point A (including the contribution from external beam and intracavitary irradiation) usually ranges between 75 and 90 Gy, depending on the clinical situation.

Use of the dose to Point A to describe intracavitary

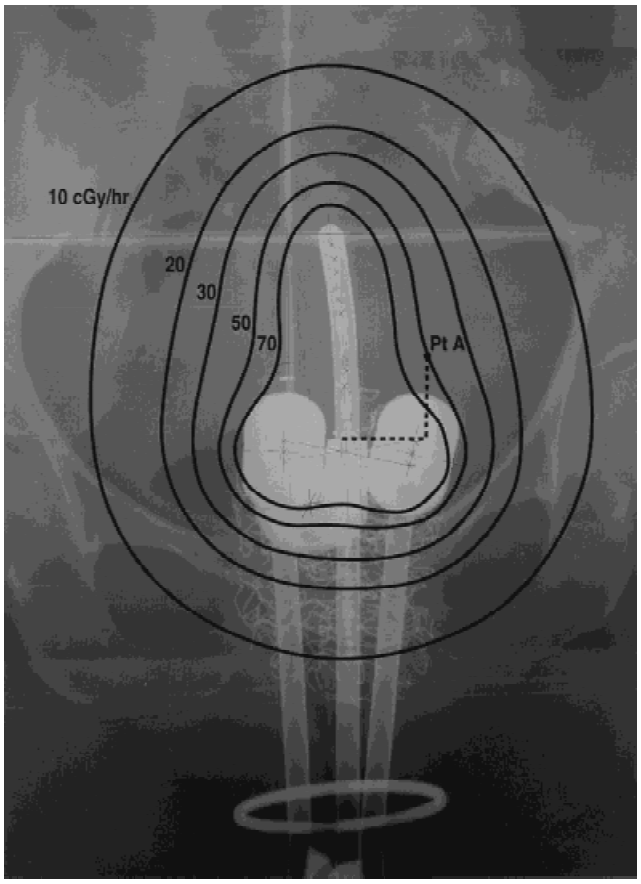

Fig. 2. Posterior–anterior view of a Fletcher-Suit-Delclos intracavitary applicator system in a patient with invasive carcinoma of the uterine cervix. The dose rates at various distances from the applicator are indicated in cGy/h. The dose from intracavitary irradiation of cervical cancer is often specified at Point A which is typically located 2 cm superior and 2 cm lateral to the external os of the cervix.

treatment intensity has been criticized because Point A bears no consistent relation to the target volume and because it lies in a region of a rapidly changing dose rate, which makes the calculated dose very sensitive to small errors in localization of the reference point. For these reasons, more than 10 years ago, the International Commission on Radiation Units and Measurements [11] recommended that the Manchester system be replaced with one that includes a description of the volume treated to 60 Gy, an assessment of the dose delivered to more distant points (measured in terms of milligram-hours or comparable units), and the dose to reference points in normal tissues. This approach is widely used in Europe but has gained only limited acceptance in the United States. Both systems have limitations and can be misleading if applied to poorly positioned intracavitary systems. In particular, a number of studies have demonstrated that calculated doses at standard reference points routinely underestimate the maximum dose to critical structures, particularly for poorly positioned intracavitary systems [12,13].

Dose Rate

Intracavitary therapy of cervical cancer is usually performed with sources that yield a dose rate (at Point A) of approximately 40–60 cGy/h. The delivery of radiation therapy at these low dose rates preferentially spares normal tissues from injury by permitting repair of sublethal radiation damage. Because the 3–4 days of hospitalization are needed to deliver an appropriate dose of low dose rate irradiation, some investigators have explored the use of intermediate dose rate brachytherapy (80–100 cGy/h). However, in a randomized trial, Haie-Meder et al. [14] reported a significant increase in complications when the dose rate was doubled from 40 to 80 cGy/h, indicating that the total dose must be reduced and the therapeutic ratio of treatment may be compromised with higher dose rates.

Computer technology has now made it possible to deliver brachytherapy at even higher dose rates (>100 cGy/min) with a high-activity ^{60}Co or ^{192}Ir source and remote afterloading. With this approach a single source is moved along a path within the tandem and vaginal applicator, stopping for precisely calculated times in various positions to generate dose distributions similar in shape to those produced with standard low dose rate applicators. High dose rate intracavitary irradiation is now being used to treat cervical cancer by a number of groups, including several in Japan, Canada, and Europe, and more recently by some groups in the United States [15–19]. Clinicians have found this approach attractive because it does not require hospitalization and may be more convenient for the patient and the physician. However, unless the dose is divided into at least 5–10 fractions, high dose rate brachytherapy may also lose the radiobiologic advantage that had contributed to the success of low dose rate treatment [20]. Advocates of high dose rate treatment disagree about the number of fractions and total dose that should be delivered. Published experiences suggest that survival rates are roughly similar to those achieved with traditional low dose rate treatment, but many of the series are small, originate from third world experiences that have poor follow-up, or are difficult to compare with low dose rate experiences because the criteria used to select patients are not well described. Two purported randomized trials [21,22] have been criticized for methodological flaws, and the use of high dose rate brachytherapy for cervical cancer continues to be a source of controversy.

Complications of Treatment

Possible acute complications of intracavitary therapy include uterine perforation, fever, and the usual risks of anesthesia. Patients are usually treated with minidose heparin to prevent thrombophlebitis during the 48–72 hours of bed rest required for low dose rate procedures.

However, the risk of thromboembolic complications is small. Dusenberry et al. [23] reported four (1.2%) thromboembolic events in 327 patients treated with brachytherapy for various gynecologic neoplasms. In a recent unpublished review of 1784 patients treated with radiotherapy for stage IB cervical cancer at M.D. Anderson Cancer Center, there were three (0.017%) suspected cases of pulmonary embolus, none of which were fatal. The risk may be somewhat greater in patients who have bulky disease on the pelvic wall.

Estimates of the risk of late complications of radical radiotherapy vary according to the treatment, method of reporting, and duration of follow-up. However, most investigators report an overall risk of major complications (requiring transfusion, hospitalization, or surgical intervention) of 5–15%. In a report from the Patterns of Care Study, Lanciano et al. [24] reported an actuarial risk of major complications of 8% at 3 years and in a separate study of 1784 patients with stage IB disease treated with radiotherapy, Eifel et al. [25] reported an actuarial risk of major complications of 7.7% at 5 years.

Rectal complications of radical radiation therapy may include bleeding, stricture, ulceration, and fistula. In the series of Eifel et al. [25] the actuarial risk of major rectal complications was 2.3% at 5 years. However, new rectal complications rarely occurred more than 3 years after treatment. Serious urinary tract complications, including hematuria, fistulae, and ureteral strictures were less frequent during the first few years after treatment but there continued to be a low risk of new urinary tract complications throughout the 25 years of the study.

Small bowel obstruction is an infrequent complication of radiotherapy in patients who have not had transperitoneal surgery and who do not receive more than 40–50 Gy of external-beam radiotherapy to the pelvis. Although the risk of small bowel obstruction is reported to be as high as 15–20% in patients who have undergone prior transperitoneal lymph node dissections, there appears to be little risk if the dissection is performed using a retroperitoneal approach.

Most patients treated with high-dose intracavitary therapy have some agglutination and telangiectasia of the apical vagina. Elderly, sexually inactive, postmenopausal women, and women who have extensive tumors treated with a high dose of irradiation may have more severe vaginal shortening; this complication can be minimized if the patients are given appropriate estrogen support and are instructed in the use of a vaginal dilator [25,26].

CANCER OF THE ENDOMETRIUM

Inoperable Endometrial Cancer

Most patients with endometrial cancer are treated initially with hysterectomy, and radiotherapy is reserved for those patients whose surgical specimens show adverse findings. However, some patients who are medically inoperable or who have extensive local disease may be treated with radiation alone. Depending on the size of the uterus, grade of the tumor, and the presence or absence of cervical or extrauterine disease, patients may be treated with intracavitary irradiation alone or combined with external beam treatment [27–30].

Patients with a very small uterine cavity may be effectively treated using a single uterine tandem that has a source of higher activity in the highest position. However, this arrangement may not deliver a sufficient dose to the myometrium for patients who have a larger uterine cavity. A number of applicator systems have been devised to improve the dose delivered to the fundus in such patients. These include the Heyman capsule or Simon afterloading systems, both of which are used to pack the uterine cavity with radium or cesium sources, improving the dose distribution to the fundus. In other cases, the desired distribution may be achieved with two tandems placed in the right and left cornu of the uterus.

Most authors report cancer-specific survival rates of 75–85% and local recurrence rates of 10–20% for patients with clinical stage I or II disease treated with radiation alone. The complication rate from this treatment is low, particularly when treatment can be accomplished with brachytherapy alone.

Vaginal Cuff Treatment

Intracavitary radiation therapy has been used to prevent disease recurrence in the vaginal cuff of patients who are at risk for such relapse after hysterectomy for endometrial cancer. In the past, most patients with grade 2 or 3 endometrial cancers received intracavitary irradiation using Heyman packings or a tandem and ovoids before hysterectomy. Preoperative intracavitary treatment was highly effective, reducing vaginal apex recurrence rates from about 10–15% to 2–3% [31,32]. However, this approach probably resulted in the unnecessary treatment of some patients who had very small, superficial tumors.

Today, clinicians usually prefer to treat most patients with initial hysterectomy, tailoring subsequent treatment to the findings from hysterectomy and surgical exploration. For patients who are at risk for vaginal cuff recurrence but who are at low risk of having regional disease, intracavitary therapy may be used to treat only the vaginal cuff. This is a simple procedure that involves the placement of a plastic domed cylinder that is usually 3–4 cm in diameter in the vagina; the cylinder is subsequently loaded with one or more radioactive sources (Fig. 3). A dose of 60–70 Gy is usually delivered to the vaginal surface in approximately 72 hours. Alternatively, high-activity sources have been used to deliver equivalent doses to the vaginal apex with high dose rate treatment divided into several fractions. Postoperative vaginal cuff

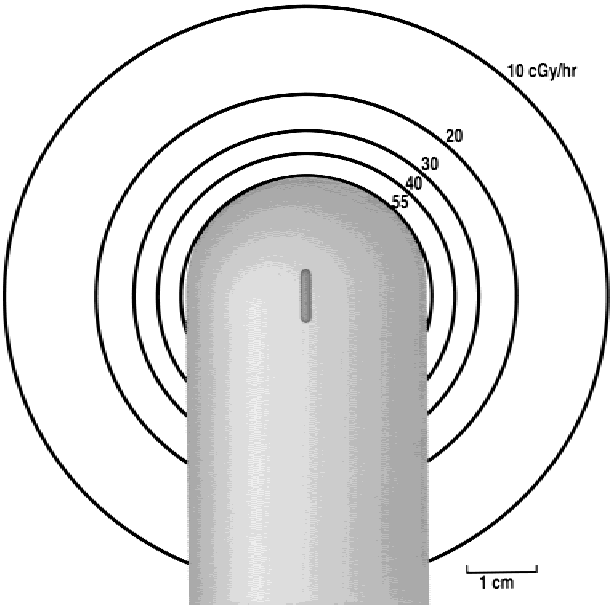

Fig. 3. Typical distribution of dose surrounding a Delclos dome cylinder used to irradiate the vaginal cuff after hysterectomy. The cylinder is loaded with a ^{137}Cs point source. Additional sources may be added to treat more of the vaginal length.

irradiation appears to prevent most vaginal apex recurrences [33–35] and because the dose of radiation decreases sharply at distances of more than a few millimeters from the vaginal surface, the risk of damage to adjacent structures is very low when appropriate doses and dose rates or fractionation schemes are used.

Sometimes intracavitary vaginal cuff irradiation is used to increase the dose to the vaginal apex in patients who are having pelvic external-beam irradiation following hysterectomy for high-risk endometrial cancer or cervical cancer. However, the benefit of this additional treatment has not been well studied. Intracavitary treatment may also be used to boost the dose to the vagina in carefully selected patients who have superficial vaginal cancers or recurrent endometrial cancers. However, because of the rapid dose gradient from the surface of a vaginal cylinder, intracavitary treatment should be reserved for lesions that are less than 3–4 mm thick. Combinations of external beam and interstitial irradiation provide more effective coverage of thicker vaginal lesions.

CONCLUSIONS

Intracavitary radiation therapy, usually in combination with tailored external-beam irradiation, permits the delivery of high doses of radiation to invasive carcinomas of the cervix with a low risk of serious morbidity. With this treatment, the majority of patients who have invasive carcinomas can be cured of their cancers, and even patients with massive tumors fixed to the pelvic wall can be cured up to 50% of the time when intracavitary treatment is emphasized and administered by experienced hands. Intravaginal and intrauterine treatment also contributes to the management of selected patients who have endometrial or vaginal carcinomas.

REFERENCES

1. League of Nations Health Organization: ‘‘Inquiry into the results of radiotherapy in cancer of the uterus. Atlas illustrating the division of cancer of the uterine cervix into four stages according to the anatomo-clinical extent of the growth.’’ Stockholm: Kungl. Boktryckeriet P. A. Norstedt & Söner, 1938.
2. Eifel PJ, Morris M, Wharton JT, et al.: The influence of tumor size and morphology on the outcome of patients with FIGO stage IB squamous cell carcinoma of the uterine cervix. Int J Radiat Oncol Biol Phys 1994;29:9–16.
3. Lowrey GC, Mendenhall WM, Million RR: Stage IB or IIA-B carcinoma of the intact uterine cervix treated with irradiation: A multivariate analysis. Int J Radiat Oncol Biol Phys 1992;24:205–210.
4. Perez CA, Grigsby PW, Nene SM, et al.: Effect of tumor size on the prognosis of carcinoma of the uterine cervix treated with irradiation alone. Cancer 1992;69:2796–2806.
5. Horiot JC, Pigneux J, Pourquier H, et al.: Radiotherapy alone in carcinoma of the intact uterine cervix according to G.H. Fletcher guidelines: A French cooperative study of 1383 cases. Int J Radiat Oncol Biol Phys 1988;14:605–611.
6. Lanciano RM, Won M, Hanks GE: A reappraisal of the International Federation of Gynecology and Obstetrics staging system for cervical cancer. Cancer 1992;69:482–487.
7. Eifel PJ, Thoms WW, Smith TL, et al.: The relationship between brachytherapy dose and outcome in patients with bulky endocervical tumors treated with radiation alone. Int J Radiat Oncol Biol Phys 1994;28:113–118.
8. Lanciano RM, Won M, Coia L, et al.: Pretreatment and treatment factors associated with improved outcome in squamous cell carcinoma of the uterine cervix: A final report of the 1973 and 1978 Patterns of Care Studies. Int J Radiat Oncol Biol Phys 1991;20: 667–676.
9. Perez CA, Kao MS: Radiation therapy alone or combined with surgery in the treatment of barrel-shaped carcinoma of the uterine cervix (Stages IB, IIA, IIB). Int J Radiat Oncol Biol Phys 1985; 11:1903–1909.
10. Lanciano RM, Martz K, Coia LR, et al.: Tumor and treatment factors improving outcome in stage III-B cervix cancer. Int J Radiat Oncol Biol Phys 1991;20:95–100.
11. International Commission on Radiation Units and Measurements: ‘‘Dose and Volume Specification for Reporting Intracavitary Therapy in Gynecology.’’ Bethesda, MD: International Commission on Radiation Units and Measurements, 1985.
12. Ling CC, Schell MC, Working KR, et al.: CT-assisted assessment of bladder and rectum dose in gynecological implants. Int J Radiat Oncol Biol Phys 1987;13:1577–1582.
13. Schoeppel SL, Fraass BA, Hopkins MP, et al.: A CT-compatible version of the Fletcher system intracavitary applicator: Clinical application and 3-dimensional treatment planning. Int J Radiat Oncol Biol Phys 1989;17:1103–1109.
14. Haie-Meder C, Kramar A, Lambin P, et al.: Analysis of complications in a prospective randomized trial comparing two brachytherapy low dose rates in cervical carcinoma. Int J Radiat Oncol Biol Phys 1994;29:1195–1197.
15. Akine Y, Arimoto H, Ogino T, et al.: High-dose-rate intracavitary irradiation in the treatment of carcinoma of the uterine cervix: Early experience with 84 patients. Int J Radiat Oncol Biol Phys 1988;14:893–898.
16. Fu KK, Phillips TL: High-dose-rate versus low-dose-rate intracavitary brachytherapy for carcinoma of the cervix. Int J Radiat Oncol Biol Phys 1990;19:791–796.
17. Newman H, James K, Smith C: Treatment of cancer of the cervix with a high-dose-rate afterloading machine (the Cathetron). Int J Radiat Oncol Biol Phys 1983;9:931–937.
18. Orton CG, Seyedsadr M, Somnay A: Comparison of high and low

dose rate remote afterloading for cervix cancer and the importance of fractionation. Int J Radiat Oncol Biol Phys 1991;21:1425–1424.
19. Stitt JA, Fowler JF, Thomadsen BR, et al.: High dose rate intracavitary brachytherapy for carcinoma of the cervix: The Madison system: I. Clinical and radiobiological considerations. Int J Radiat Oncol Biol Phys 1992;24:383–386.
20. Eifel PJ: High-dose-rate brachytherapy for carcinoma of the cervix: High tech or high risk? Int J Radiat Oncol Biol Phys 1992; 24:383–386.
21. Patel FD, Sharma SC, Neigi PS, et al.: Low dose rate vs. high dose rate brachytherapy in the treatment of carcinoma of the uterine cervix: a clinical trial. Int J Radiat Oncol Biol Phys 1993;28:335–341.
22. Shigematsu Y, Nishiyama K, Masaki N, et al.: Treatment of carcinoma of the uterine cervix by remotely controlled afterloading intracavitary radiotherapy with high-dose rate: A comparative study with a low-dose rate system. Int J Radiat Oncol Biol Phys 1983;9:351–356.
23. Dusenbery KE, Carson LF, Potish RA: Perioperative morbidity and mortality of gynecologic brachytherapy. Cancer 1991;67: 2786–2790.
24. Lanciano RM, Martz D, Montana GS, et al.: Influence of age, prior abdominal surgery, fraction size, and dose on complications after radiation therapy for squamous cell cancer of the uterine cervix. A Patterns of Care Study. Cancer 1992;69:2124–2130.
25. Eifel PJ, Levenback C, Wharton JT, et al.: Time course and incidence of late complications in patients treated with radiation therapy for FIGO stage IB carcinoma of the uterine cervix. Int J Radiat Oncol Biol Phys 1995;32:1289–1300.
26. Bruner DW, Lanciano R, Keegan M, et al.: Vaginal stenosis and sexual function following intracavitary radiation for the treatment of cervical and endometrial carcinoma. Int J Radiat Oncol Biol Phys 1993;27:825–830.
27. Grigsby P, Kuske R, Perez C, et al.: Medically inoperable stage I adenocarcinoma of the endometrium treated with radiotherapy alone. Int J Radiat Oncol Biol Phys 1987;13:483–488.
28. Kupelian PA, Eifel PJ, Tornos C, et al.: Treatment of endometrial carcinoma with radiation therapy alone. Int J Radiat Oncol Biol Phys 1993;27:817–824.
29. Lehoczky O, Bosze P, Ungar L, et al.: Stage I endometrial carcinoma: Treatment of nonoperable patients with intracavitary radiation therapy alone. Gynecol Oncol 1991;43:211–216.
30. Rose PG, Baker S, Kern M, et al.: Primary radiation therapy for endometrial carcinoma: A case controlled study. Int J Radiat Oncol Biol Phys 1993;27:585–590.
31. Jones HW: Treatment of adenocarcinoma of the endometrium. Obstet Gynecol Surv 1975;30:147–169.
32. Underwood PB, Lutz MH, Kreutner A, et al.: Carcinoma of the endometrium: Radiation followed immediately by operation. Am J Obstet Gynecol 1977;128:86–95.
33. Elliott P, Green D, Coates A, et al.: The efficacy of postoperative vaginal irradiation in preventing vaginal recurrence in endometrial cancer. Int J Gynecol Cancer 1994;4:84–93.
34. Marchetti DL, Piver MS, Tuskada Y, et al.: Prevention of vaginal recurrence of stage I endometrial adenocarcinoma with postoperative vaginal radiation. Obstet Gynecol 1986;67:399–402.
35. Piver MS, Hempling RE: A prospective trial of postoperative vaginal radium/cesium for grade 1–2 less than 50% myometrial invasion and pelvic radiation therapy for grade 3 or deep myometrial invasion in surgical stage I endometrial adenocarcinoma. Cancer 1990;66:1133–1138.